

Fig. 1
(prior art)

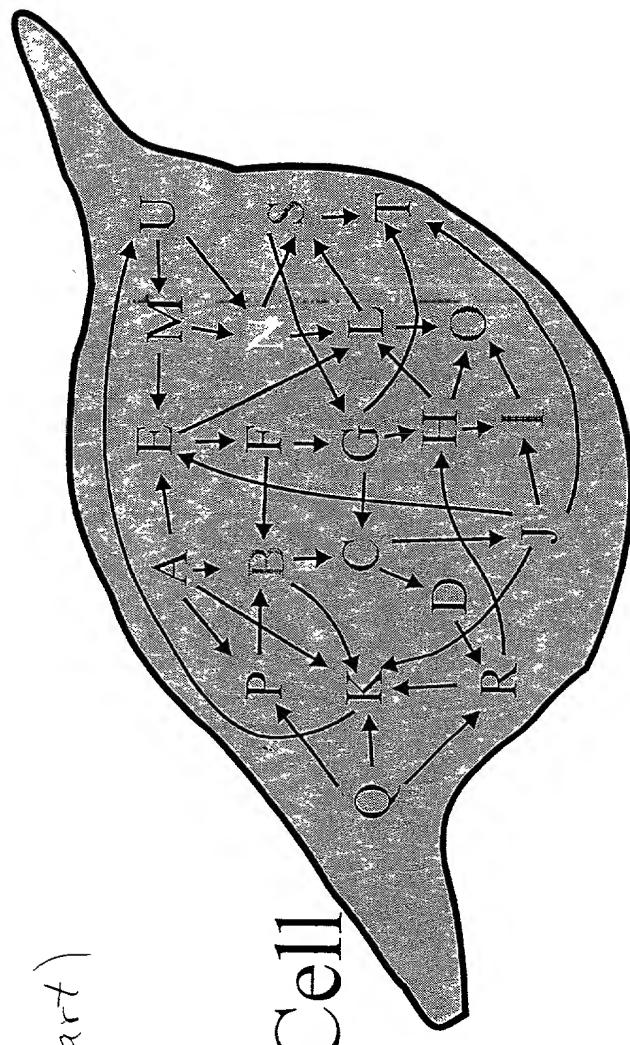


Fig. 2 (prior art)

MAP Kinase/Phosphoinositide/ PI3 Kinase Pathways in the Network

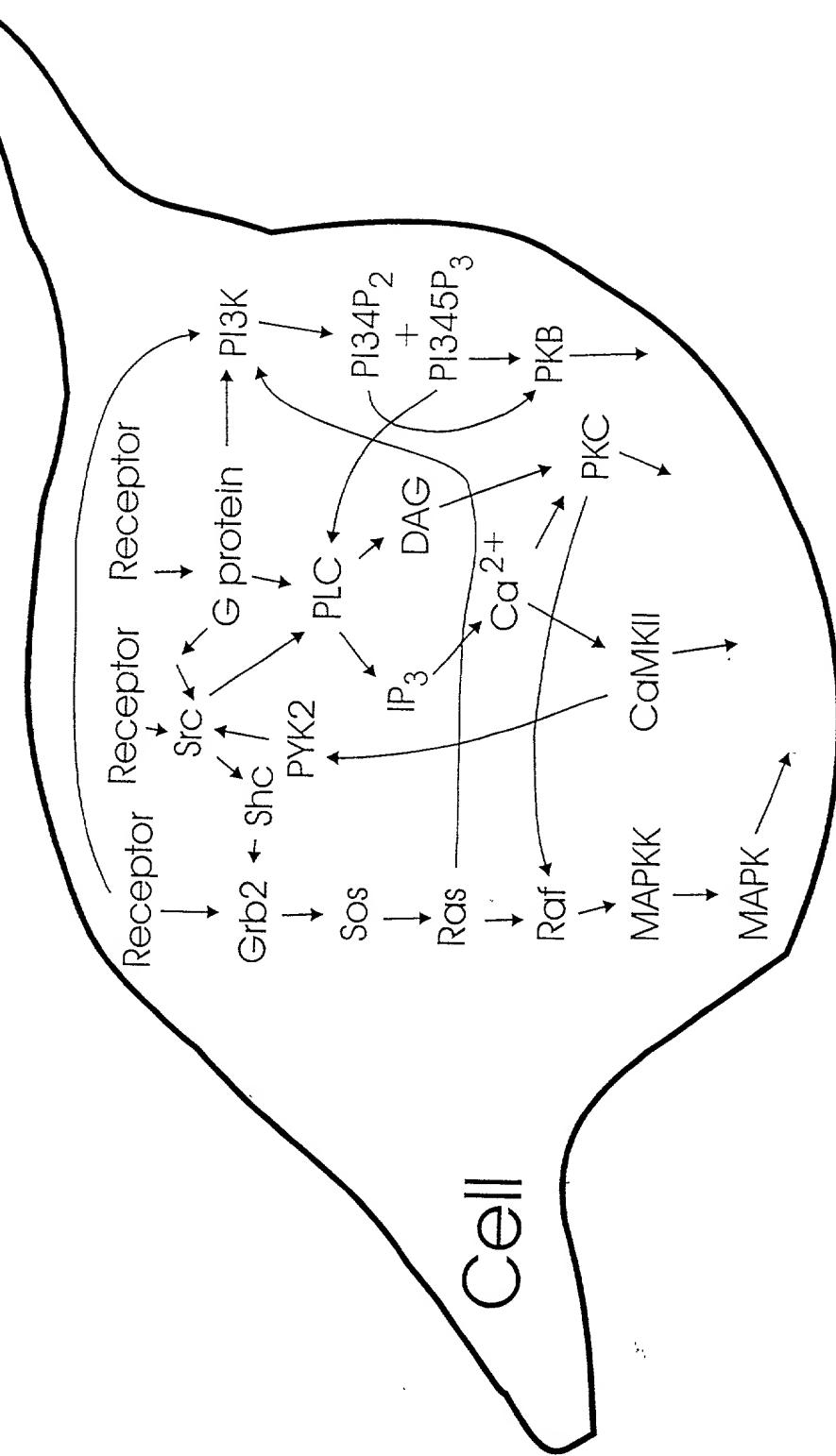


Fig. 3

(prior α_{r+})

Measurement of Kinase Activation (Current Technology)

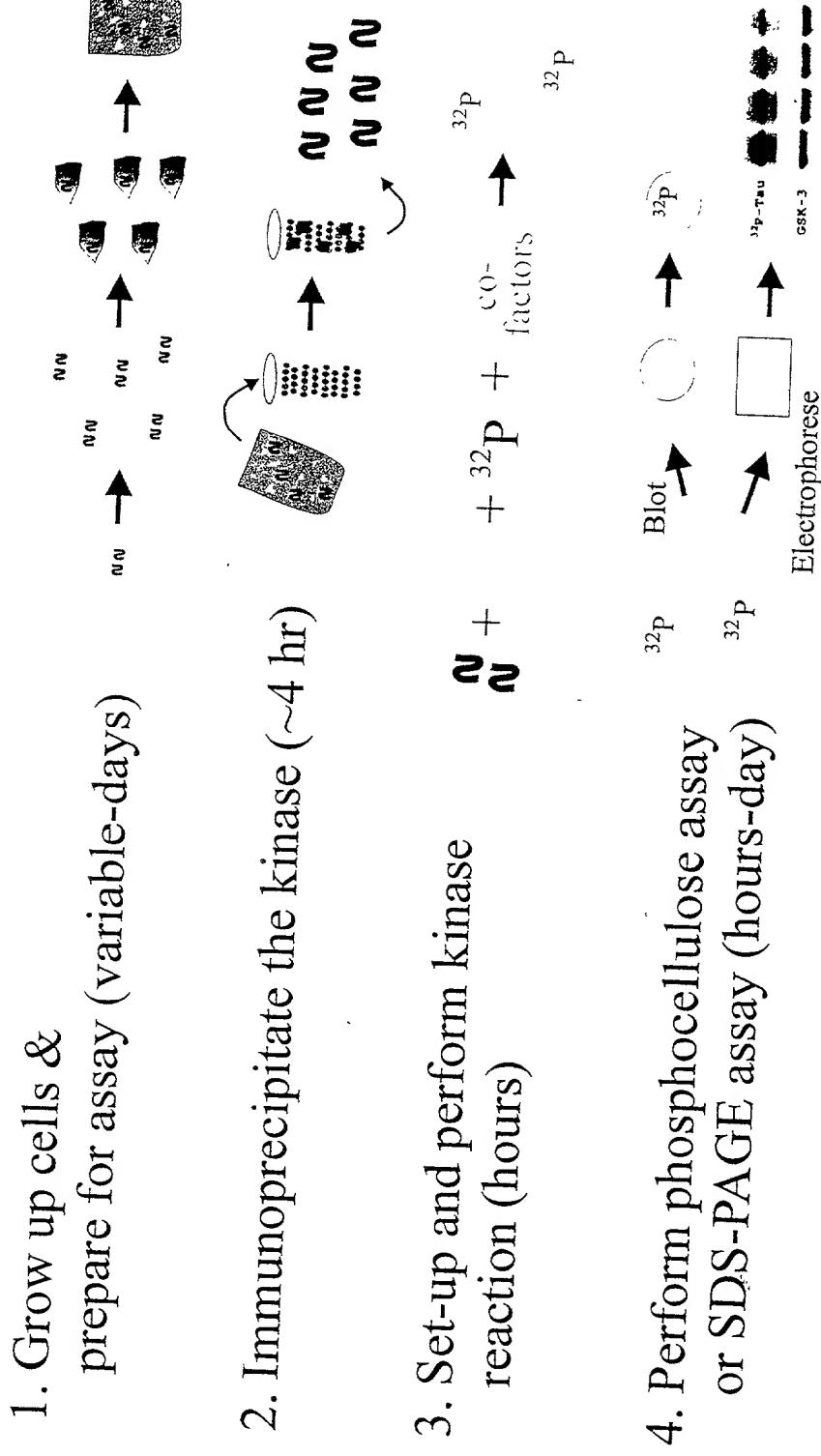
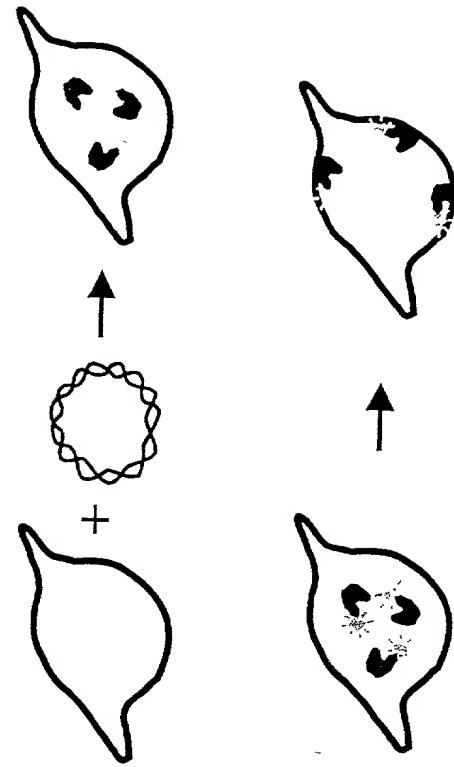


Fig. 4

(prior art) Measurement of Protein Location (via GFP Tag)

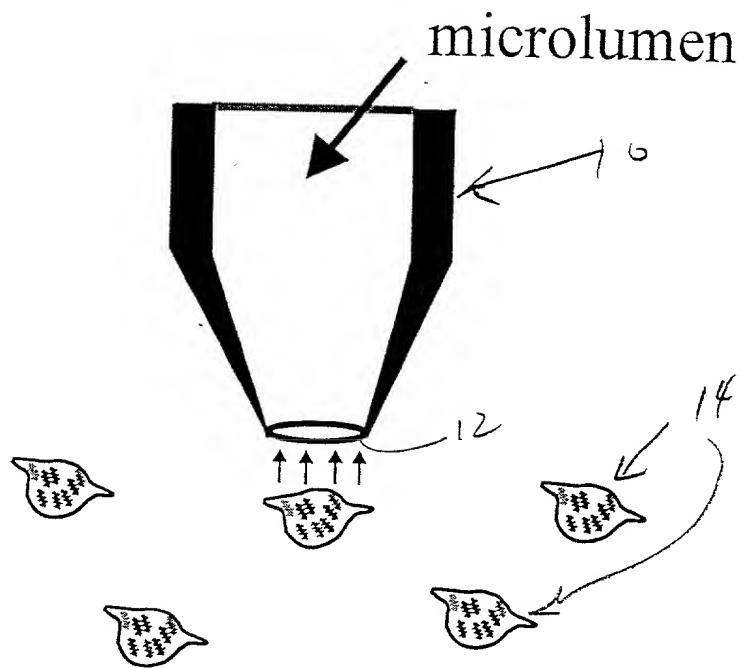
1. Develop stably transfected cell lines carrying the overexpressed GFP-tagged protein
2. Fluorescent imaging and pattern recognition
3. Infer protein activity from location



Assay Time ~Minutes

Fig. 5A

Single



Multiple

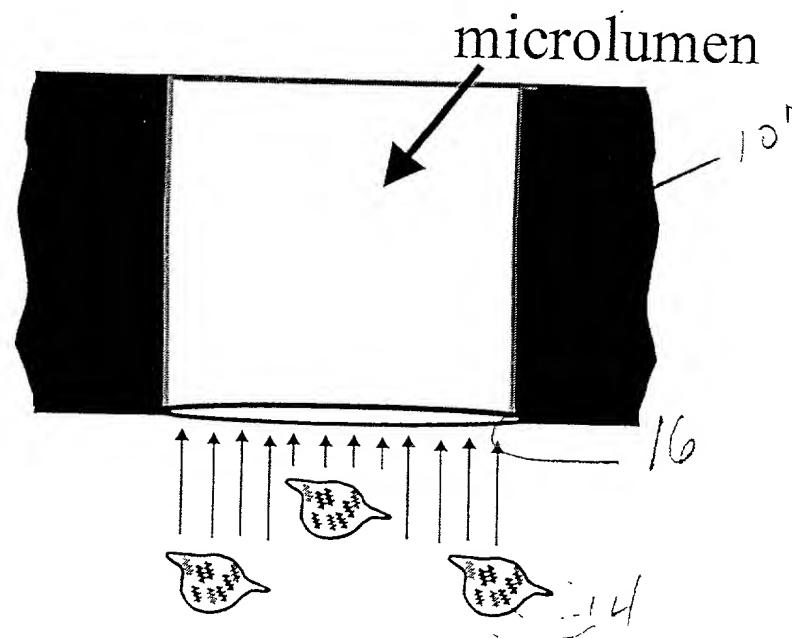
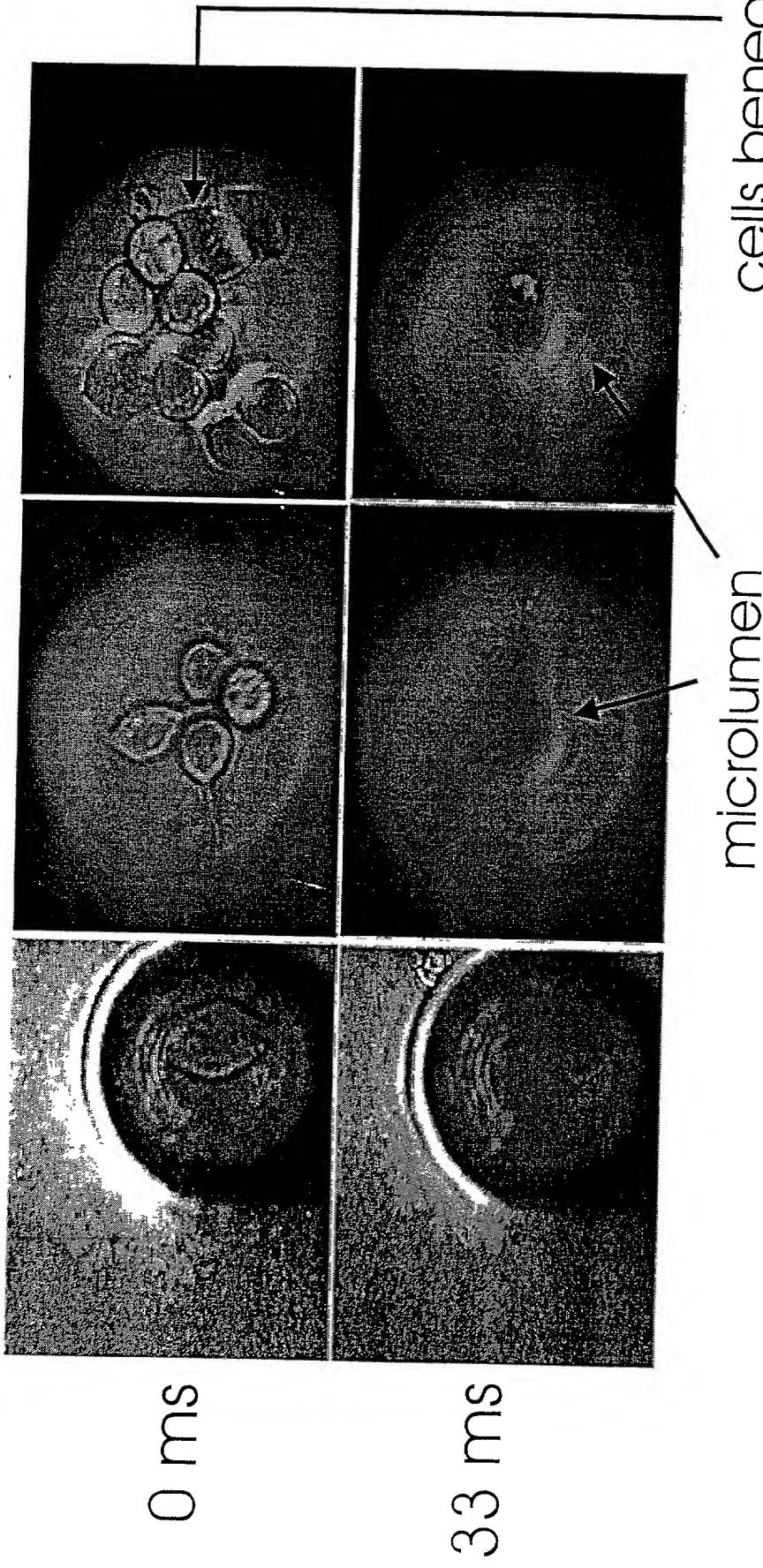


Fig. 5B

Performing "Population
Average" Measurements

1 Cell 4 Cells 10 Cells



cells beneath
a microlumen

Single Cells or Population Averages

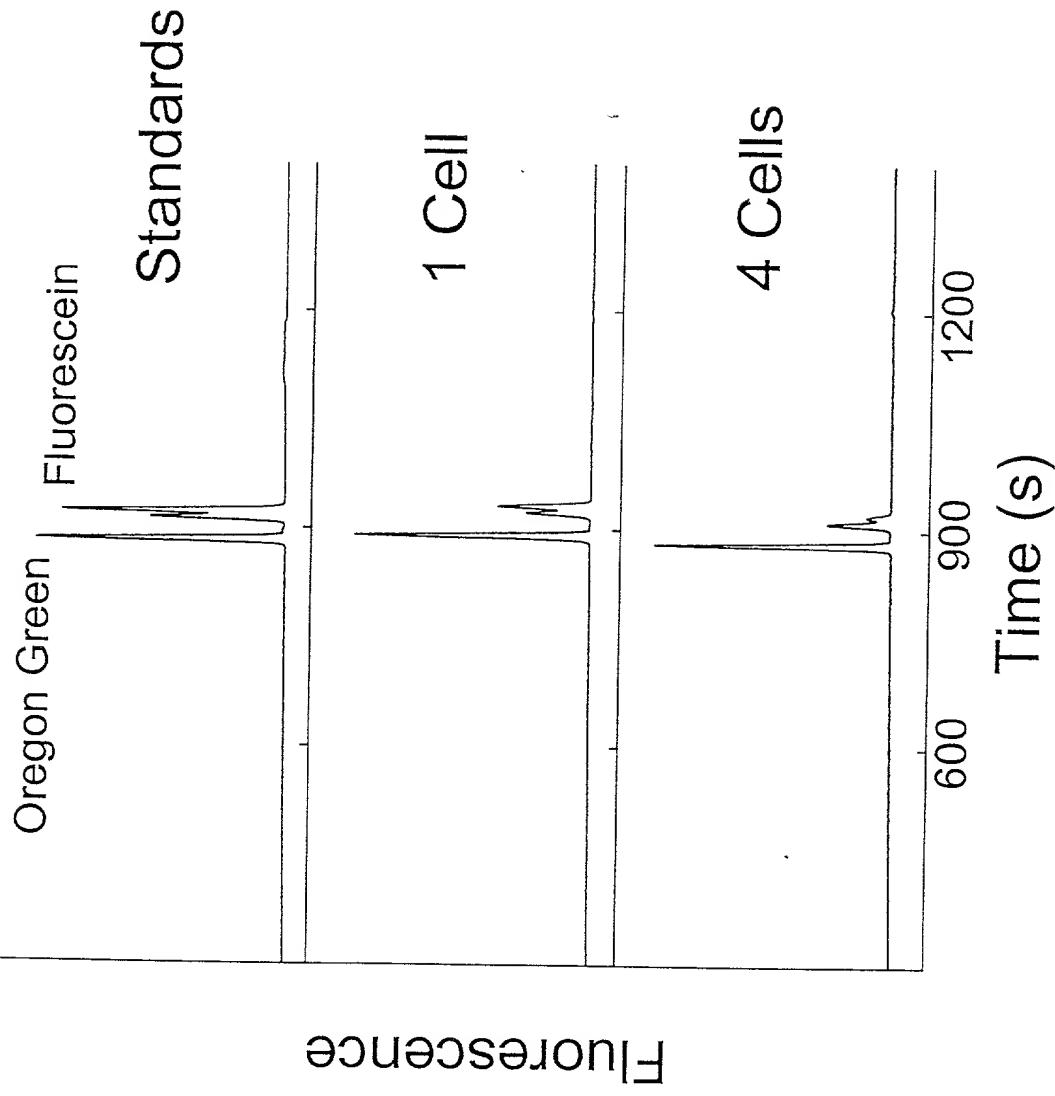


Fig. 5C

Fig. 6A Sampling a Portion of a Cell

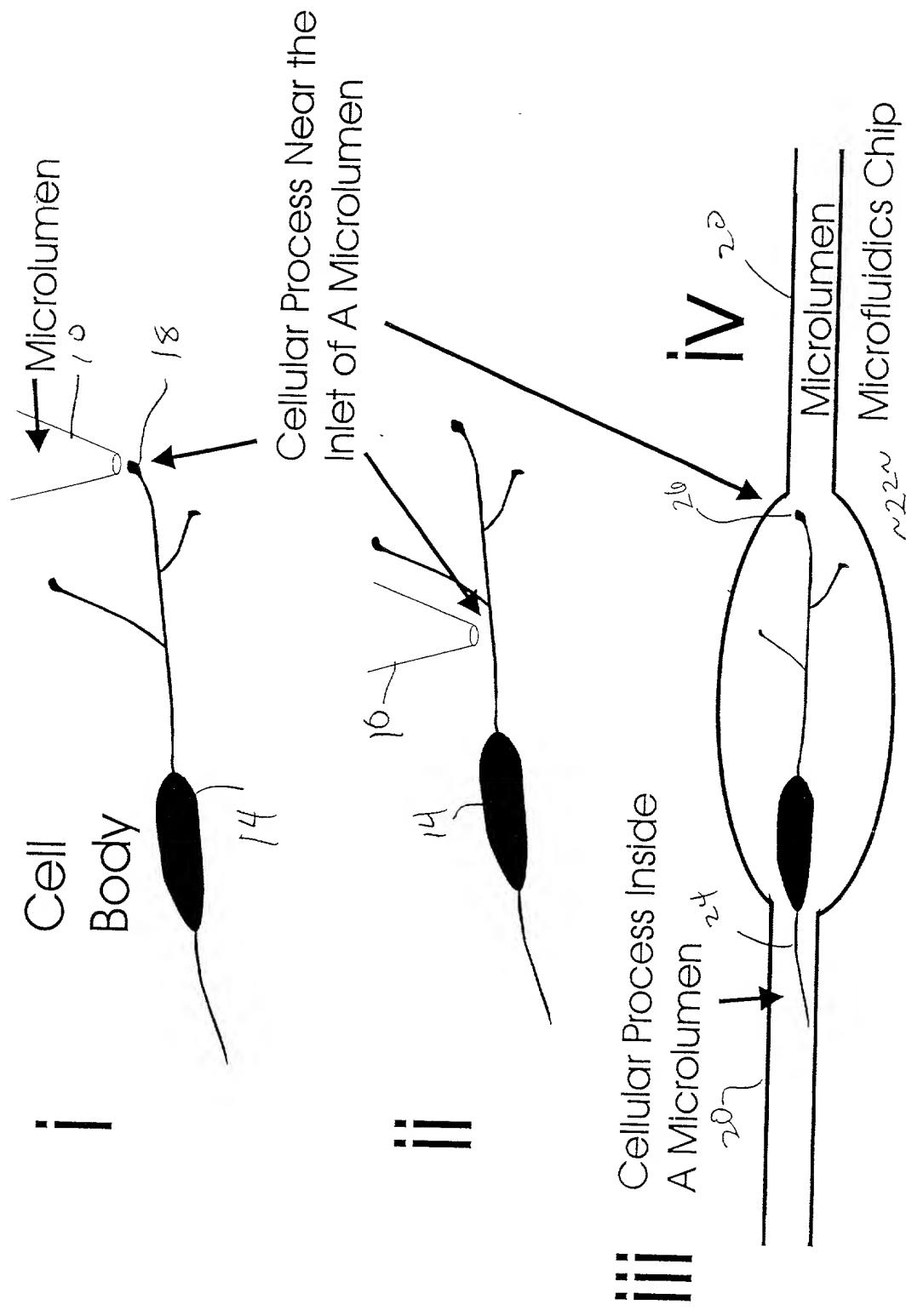


Fig. 6B

Sampling the Contents of a Neuronal Process

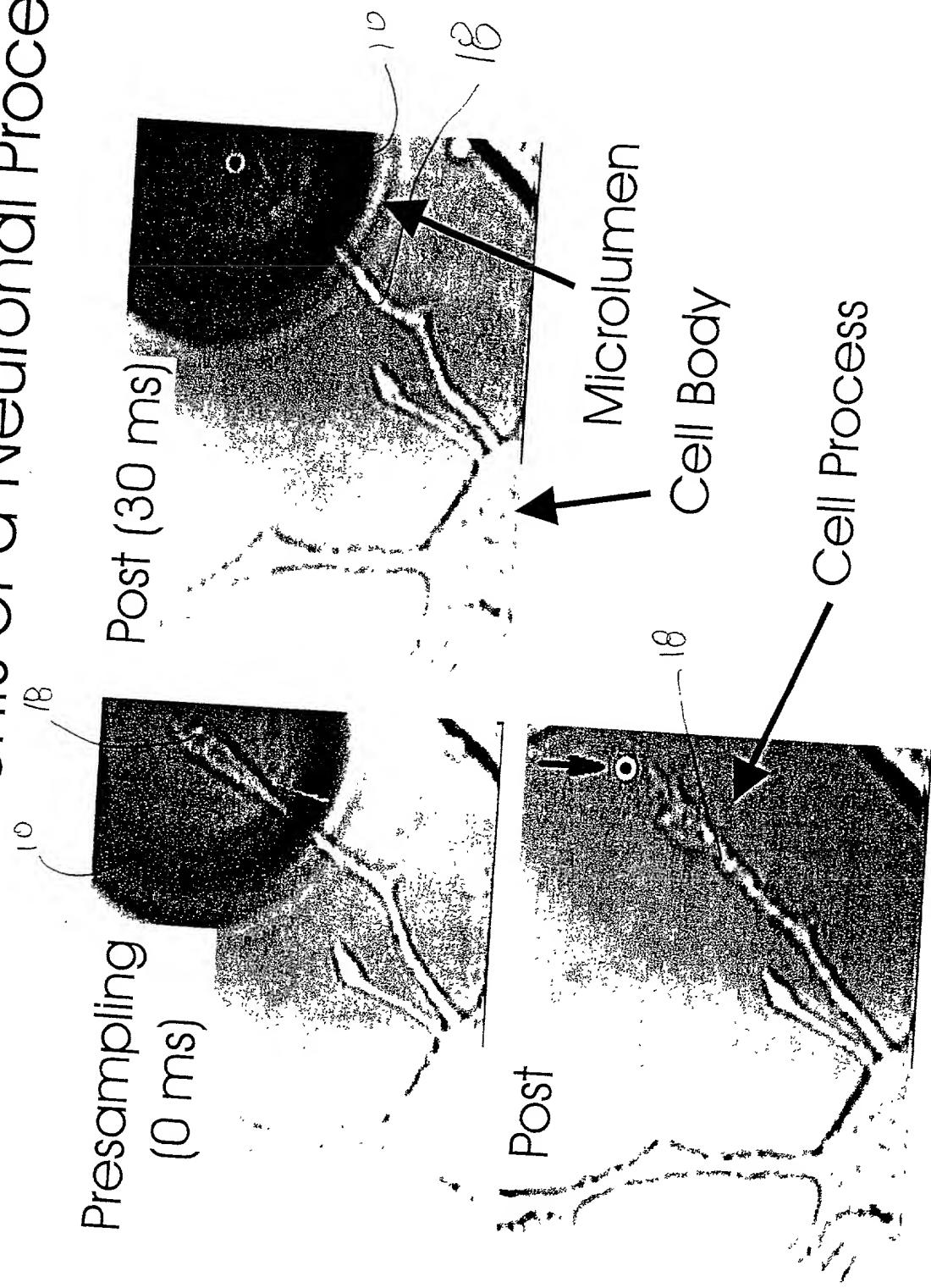


Fig. 6C

Analyzing A Neuronal Process

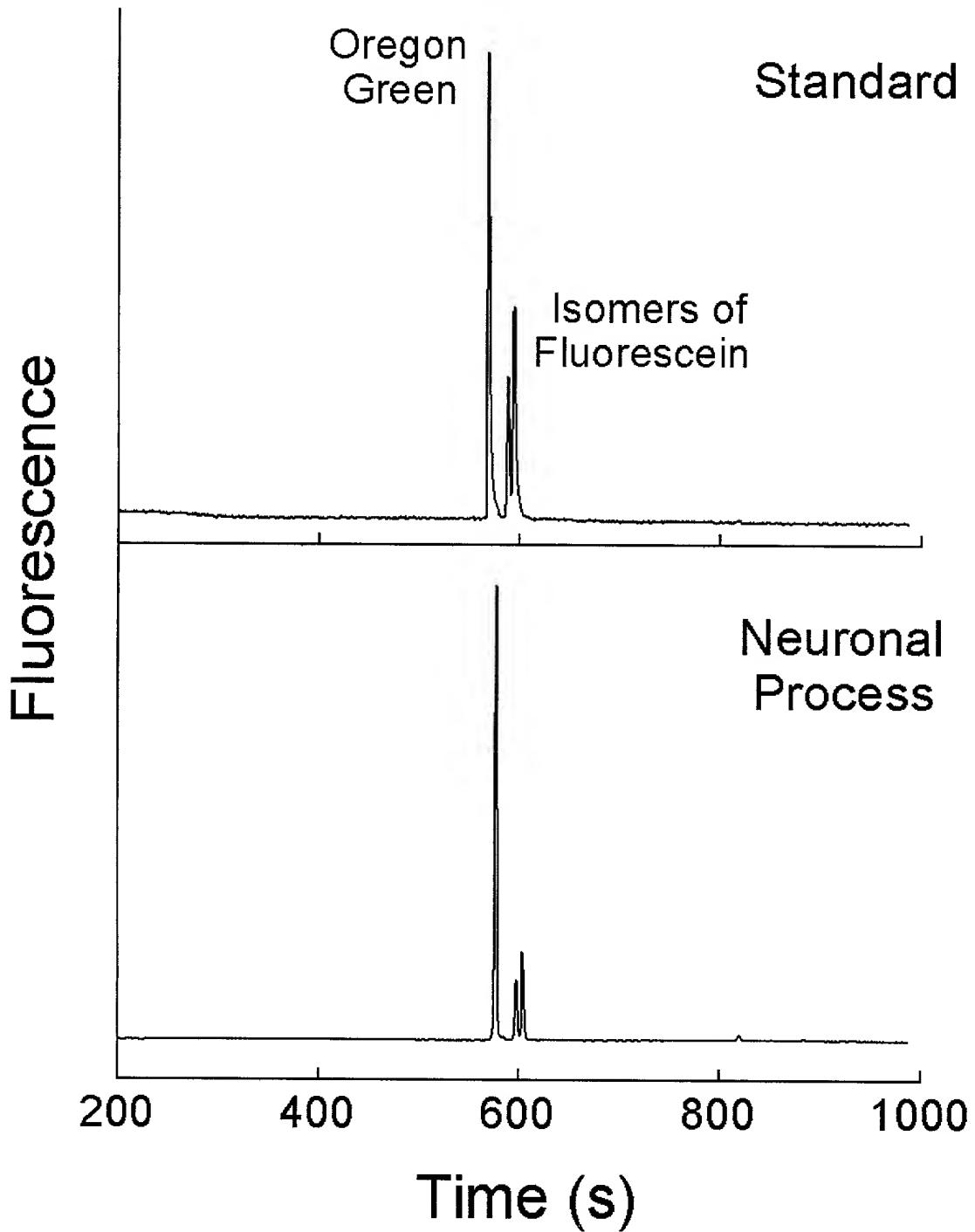


Fig. 7

Cell Assay

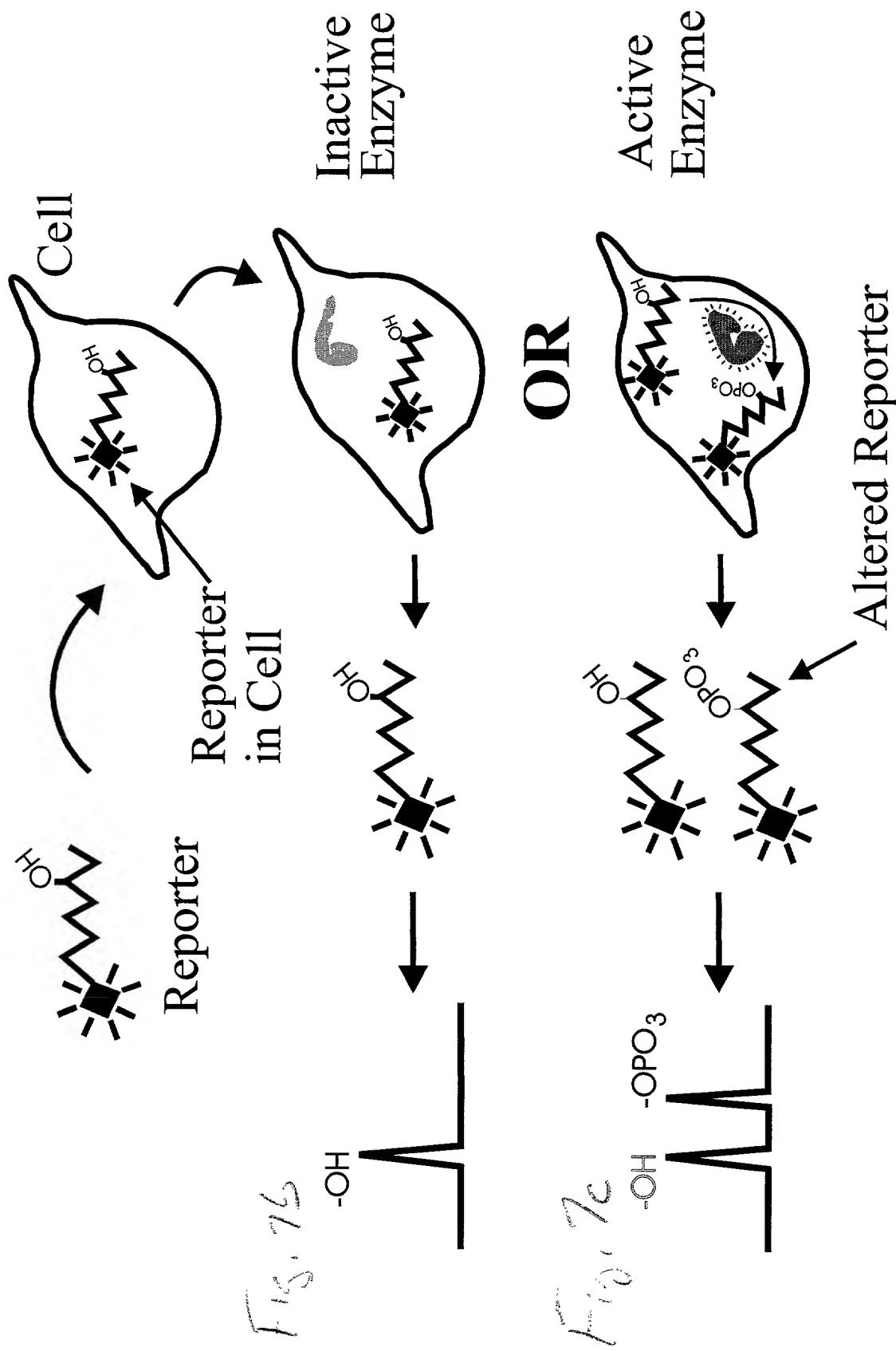


Fig. 8

Loading Single Cells With Enzyme Substrates

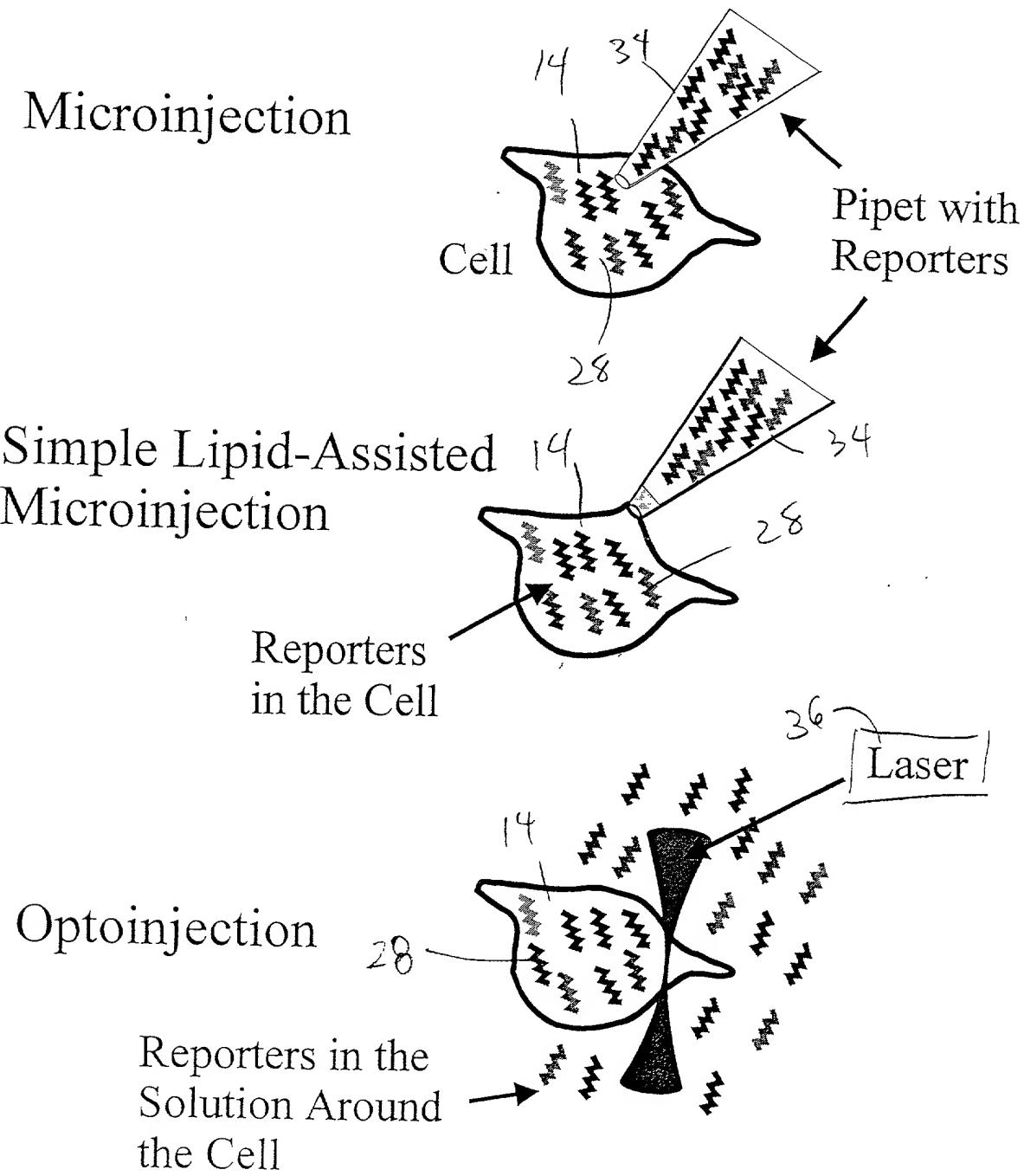
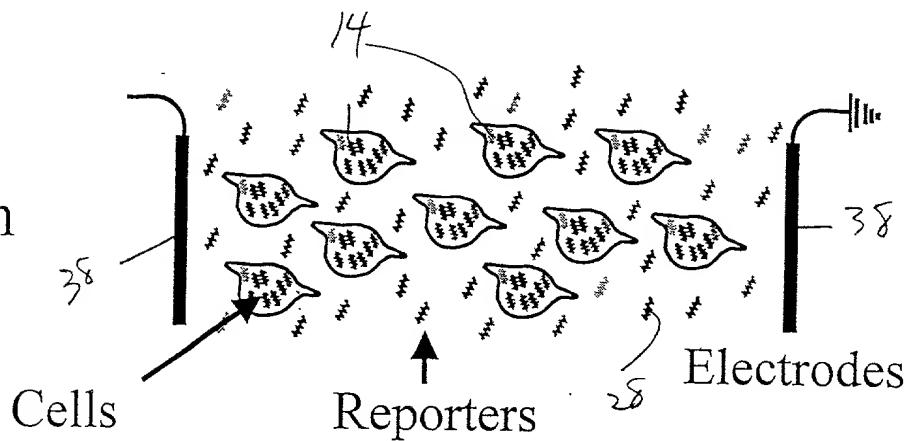
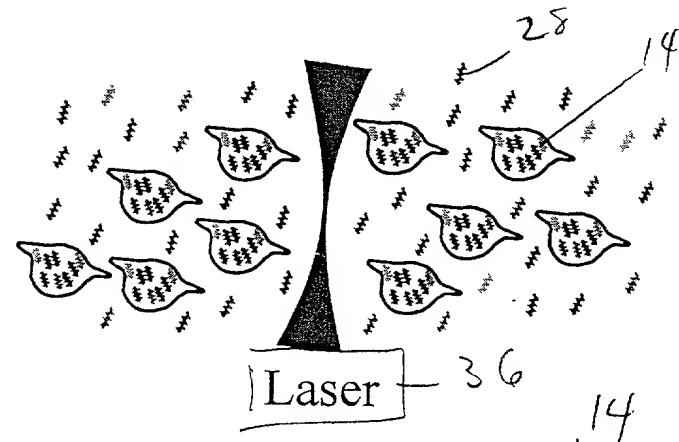


Fig. 9 Loading Multiple Cells With Enzyme Substrates

Electroporation



Optoporation



Passive Techniques

Pinocytosis

Vesicle Fusion

Membrane-Permeant
Substrates

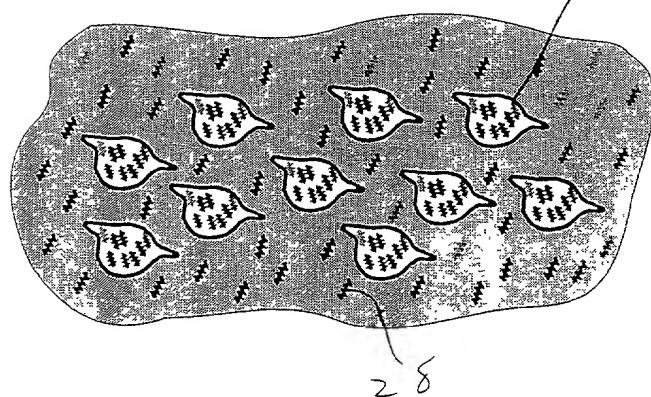


Fig. 10

Nuclear-Localized Substrate for PKC
Fluorescence Image Transmitted Light Image

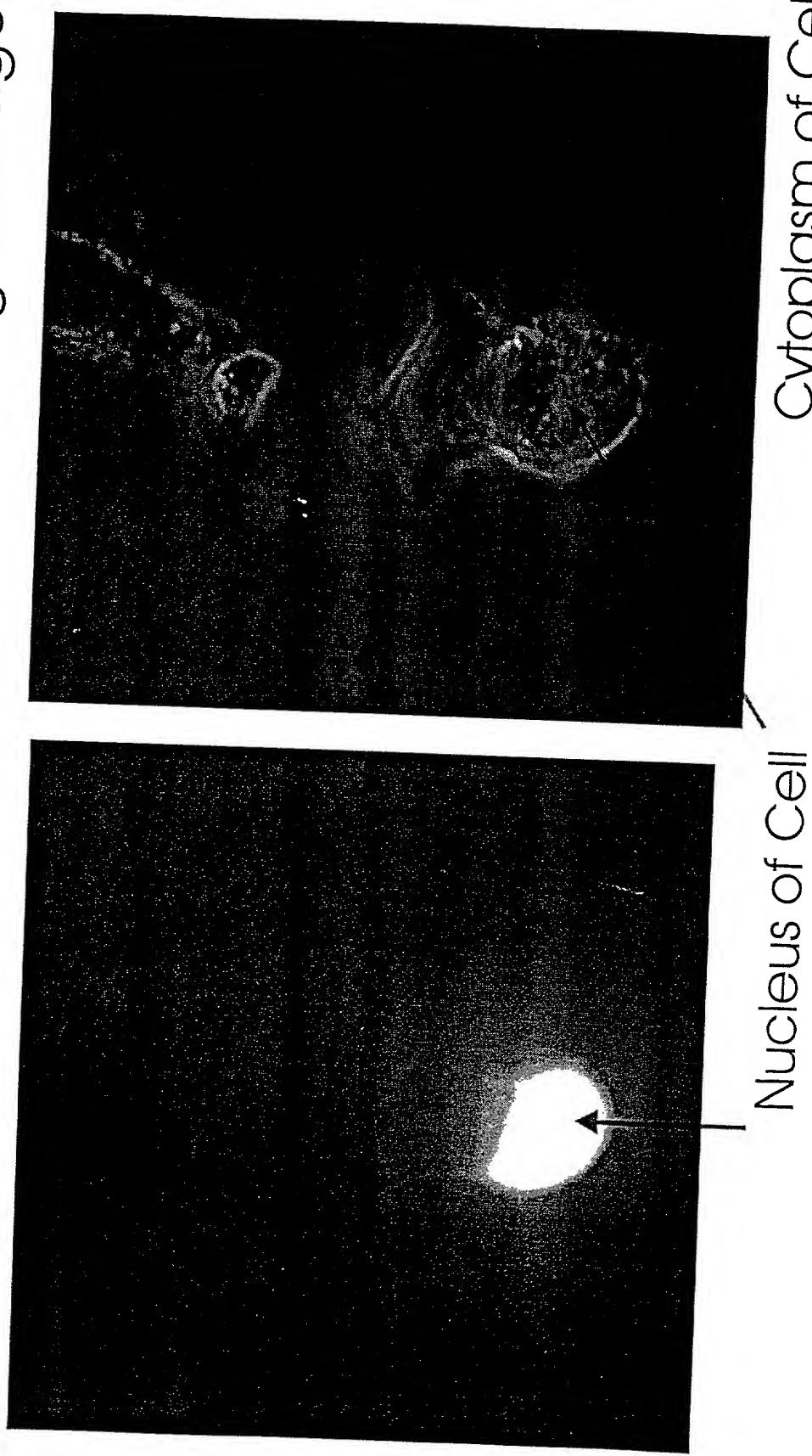


Fig. 11

Coupling to Other Technologies

Proteomics

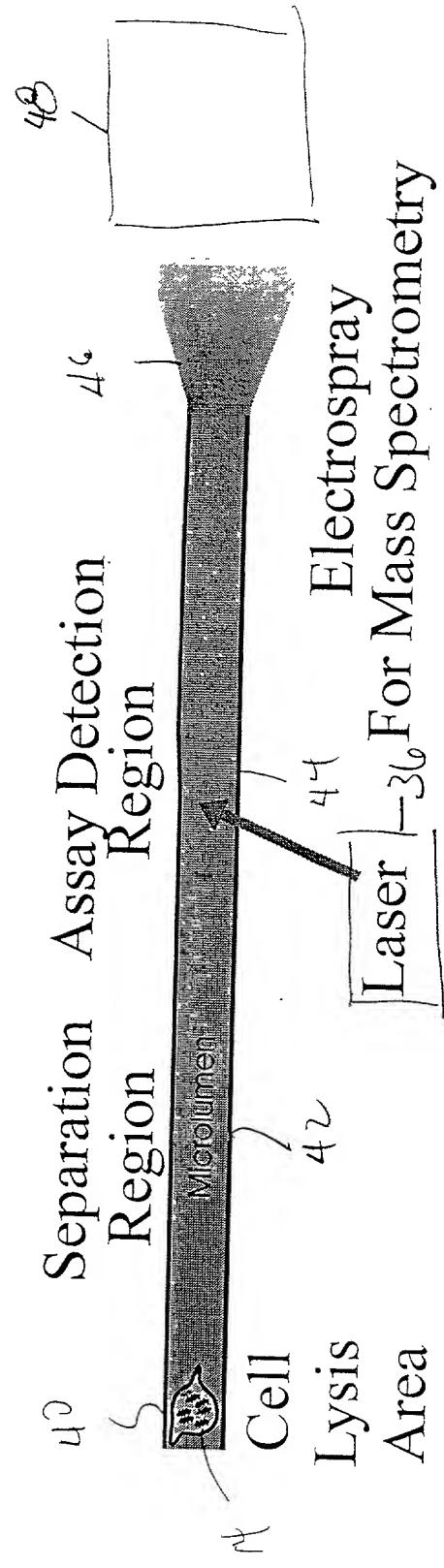


Fig. 12A

Coupling to Other Technologies Genomics

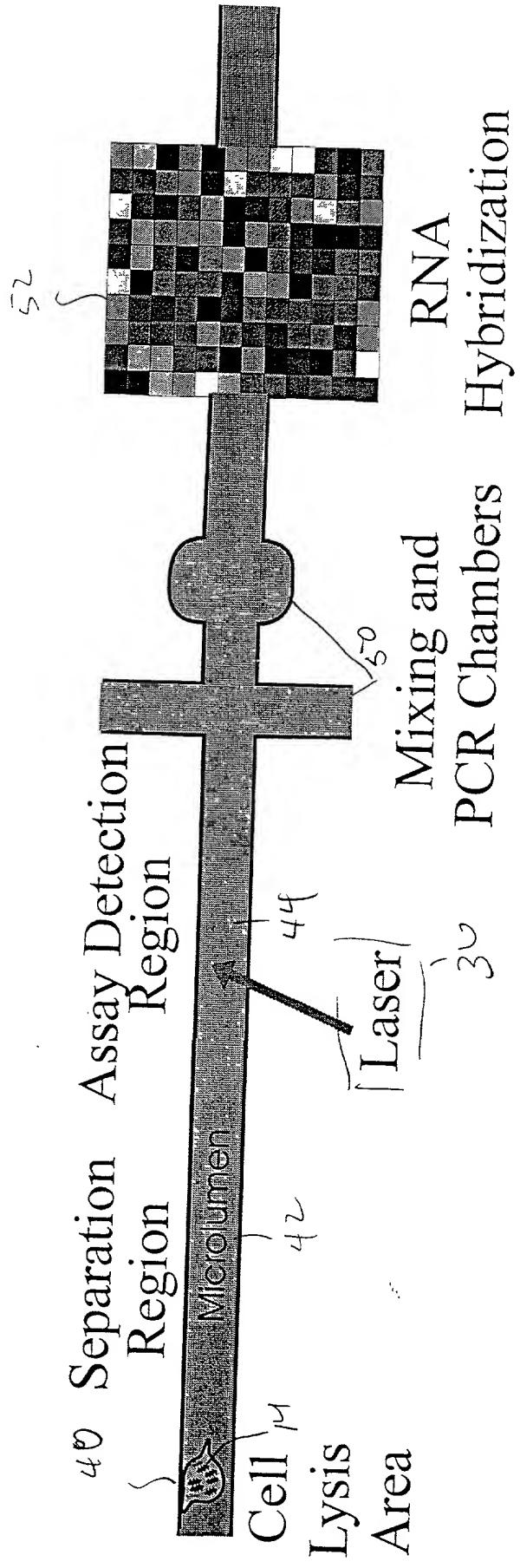


Fig. 12B

SIGNAL TRANSDUCTION MICROCHIP

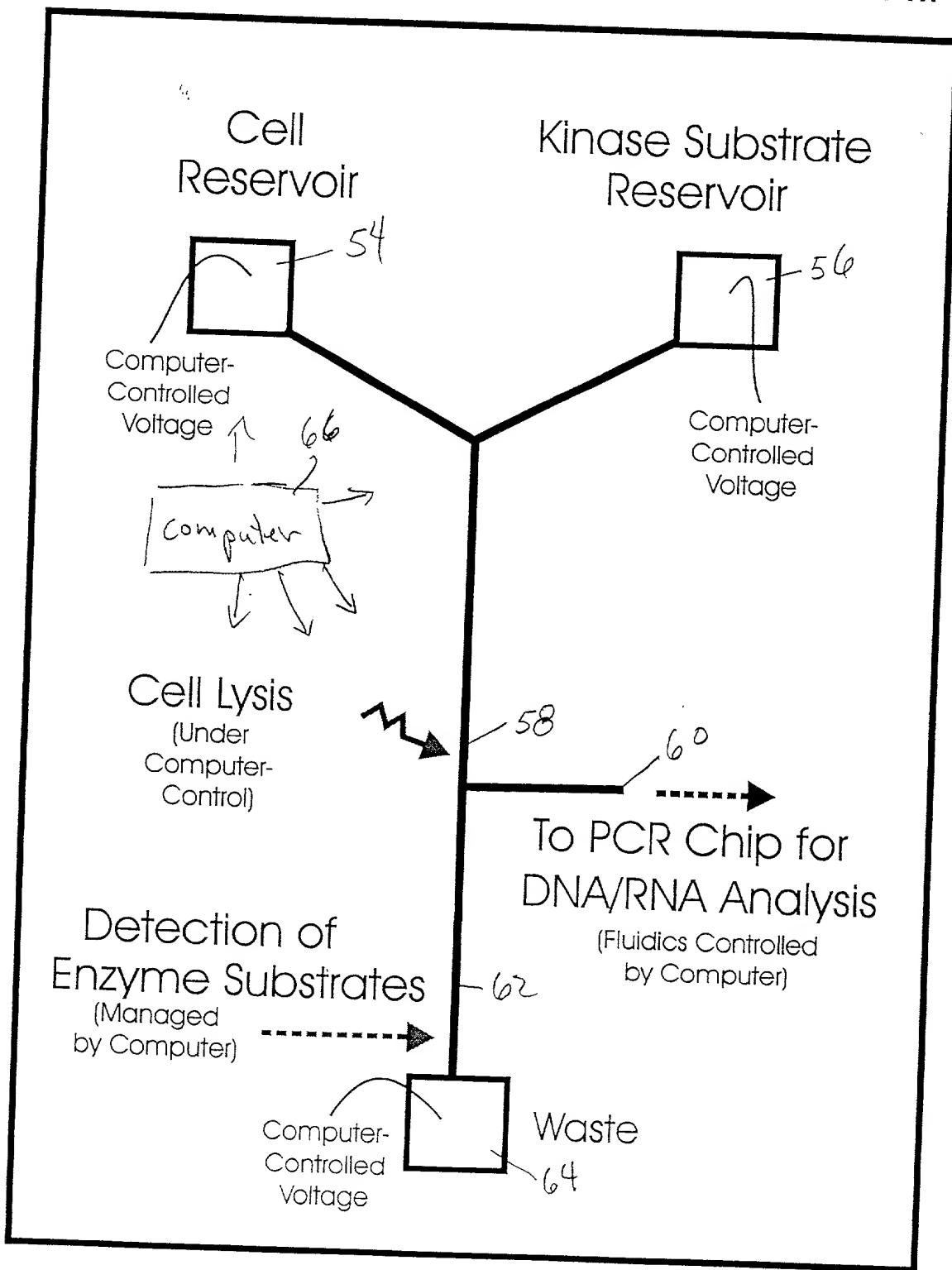


Fig. 13

Coupling to Other Technologies

Flow Cytometry

Cell
Interrogation

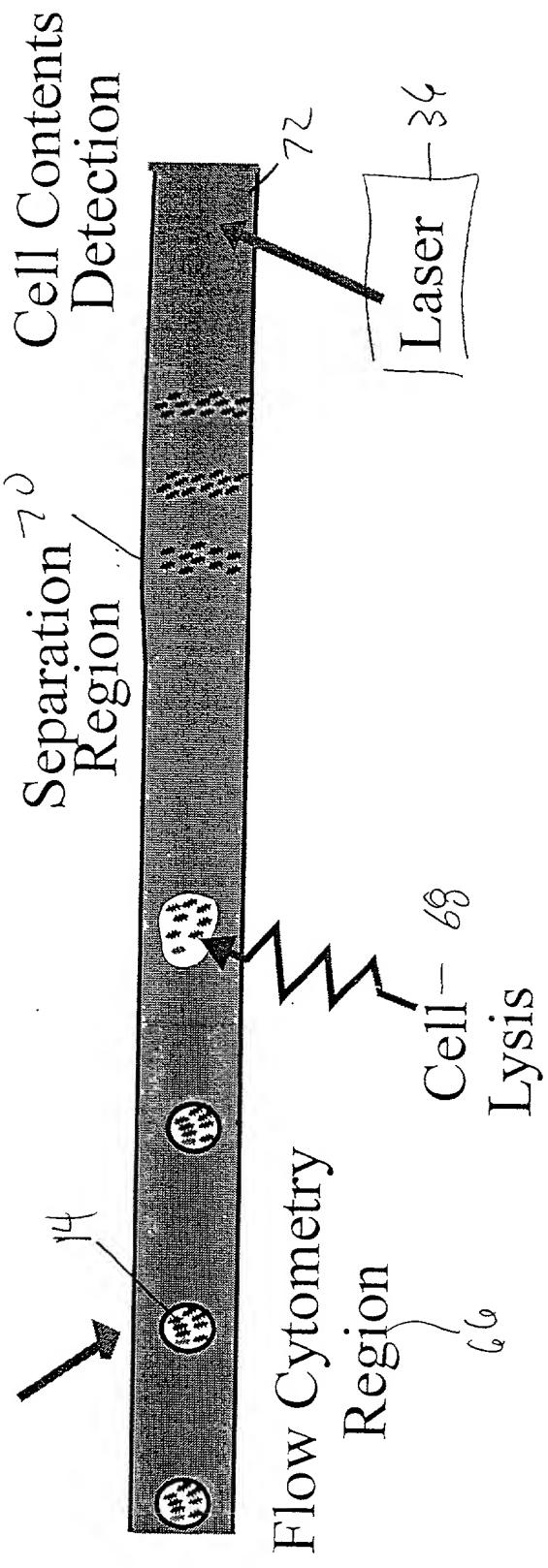
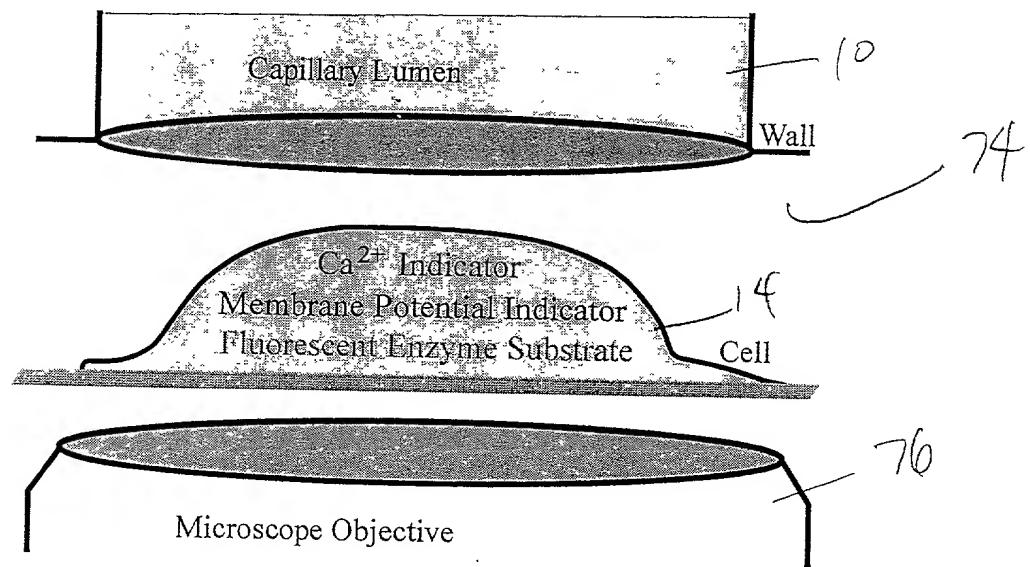


Fig. 14

Integration With Other Cellular Analysis Methods

Fluorescence Imaging



Patch Clamp

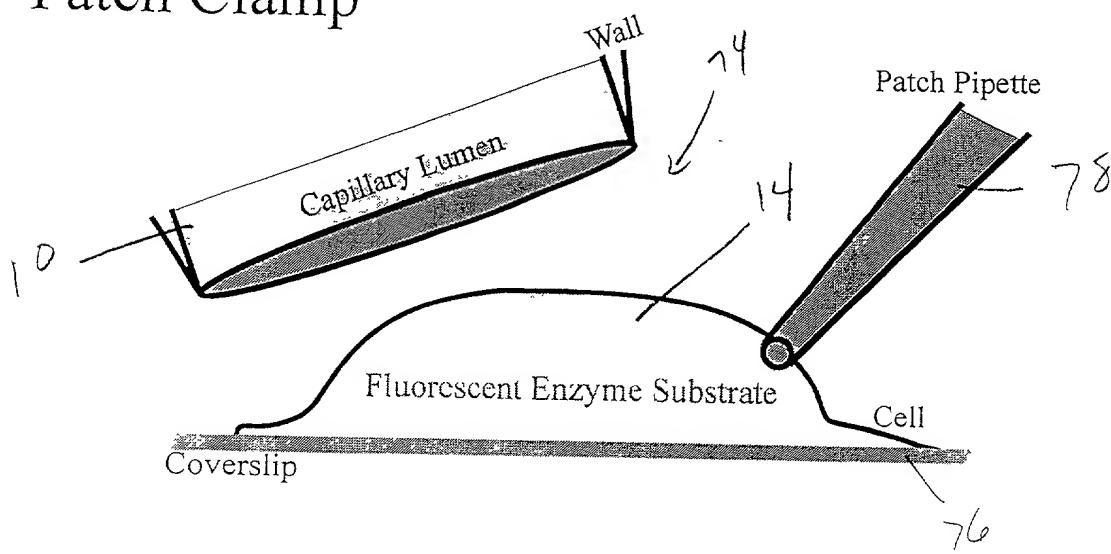


Fig. 15A

Profiling Signal Transduction Pathways
in Cells with Four Reporters

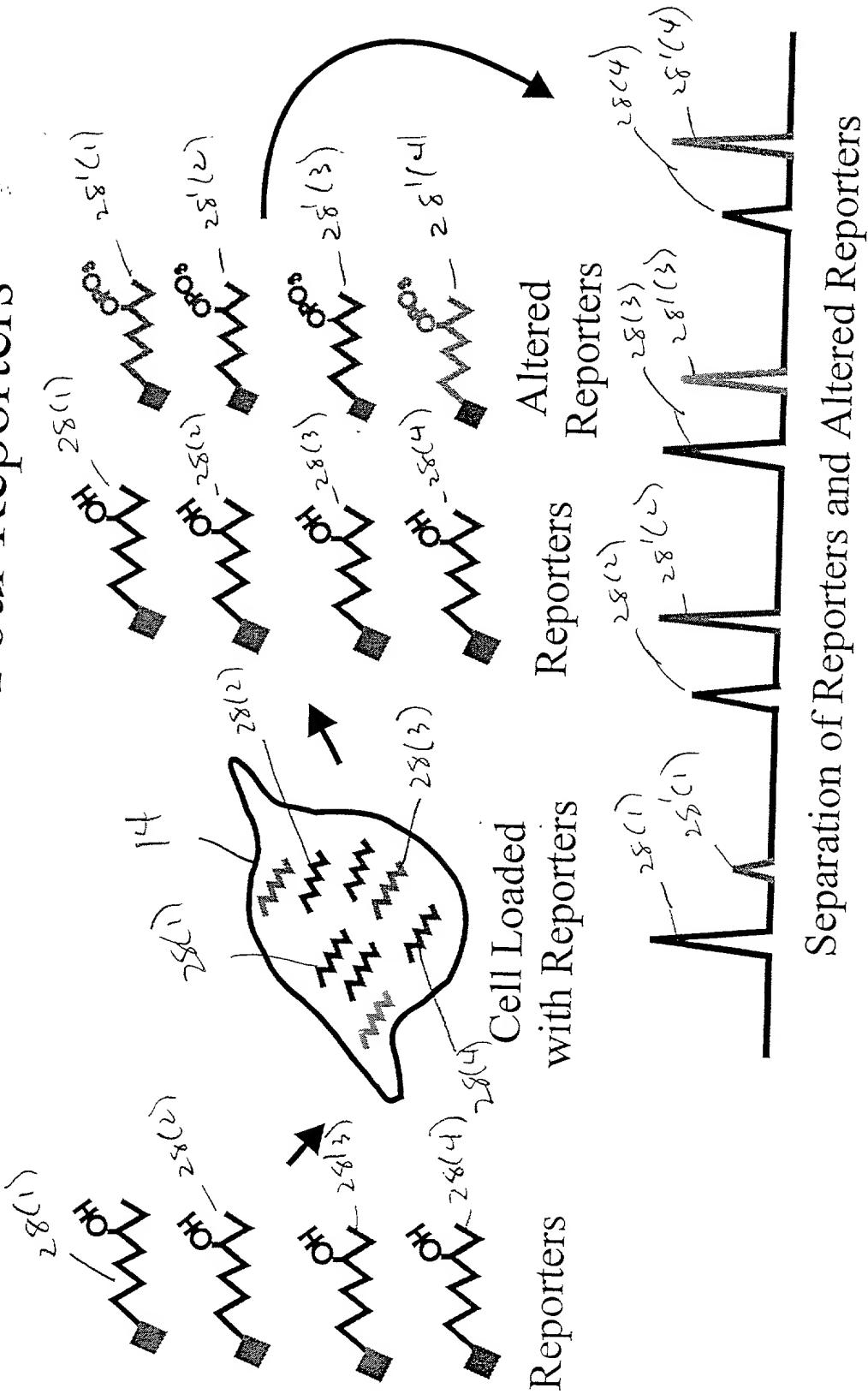


Fig. 15B

Profiling Signal Transduction Pathways
in Cells with Three Reporters

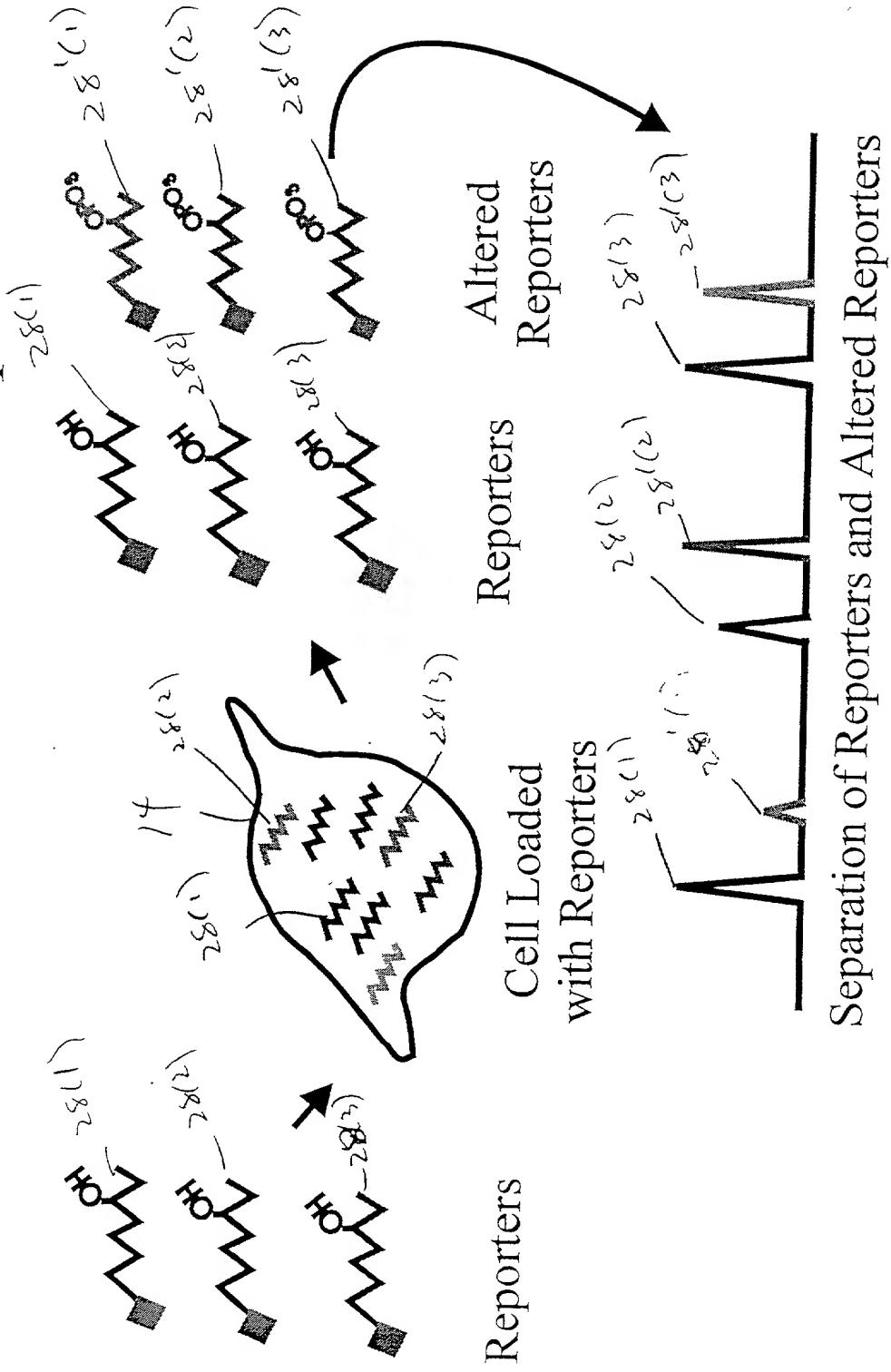


Fig. 16

Profiling Signal Transduction Pathways
in Cells with Five Reporters

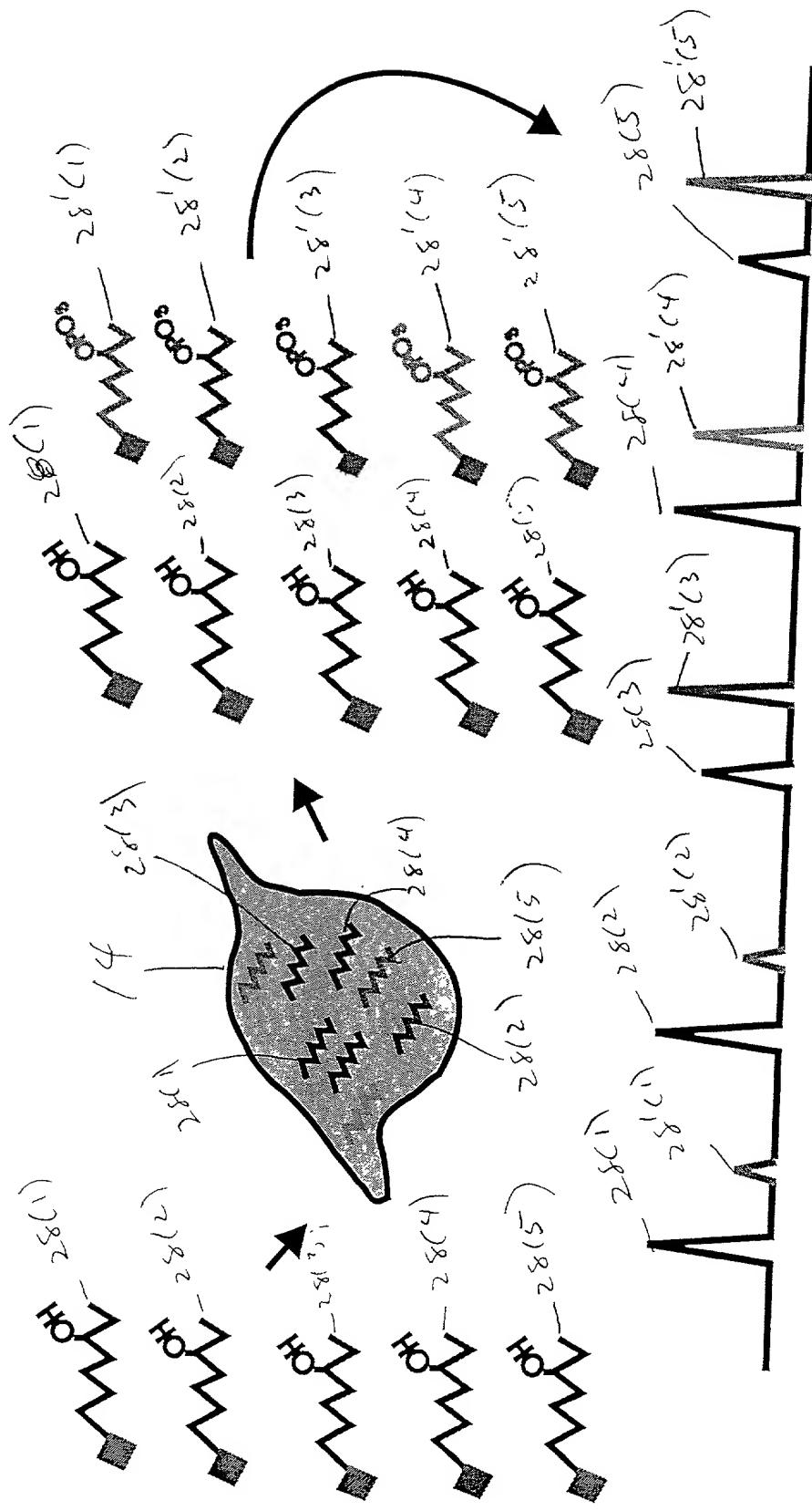


Fig. 17

Profiling Signal Transduction Pathways
in Cells with Ten Reporters

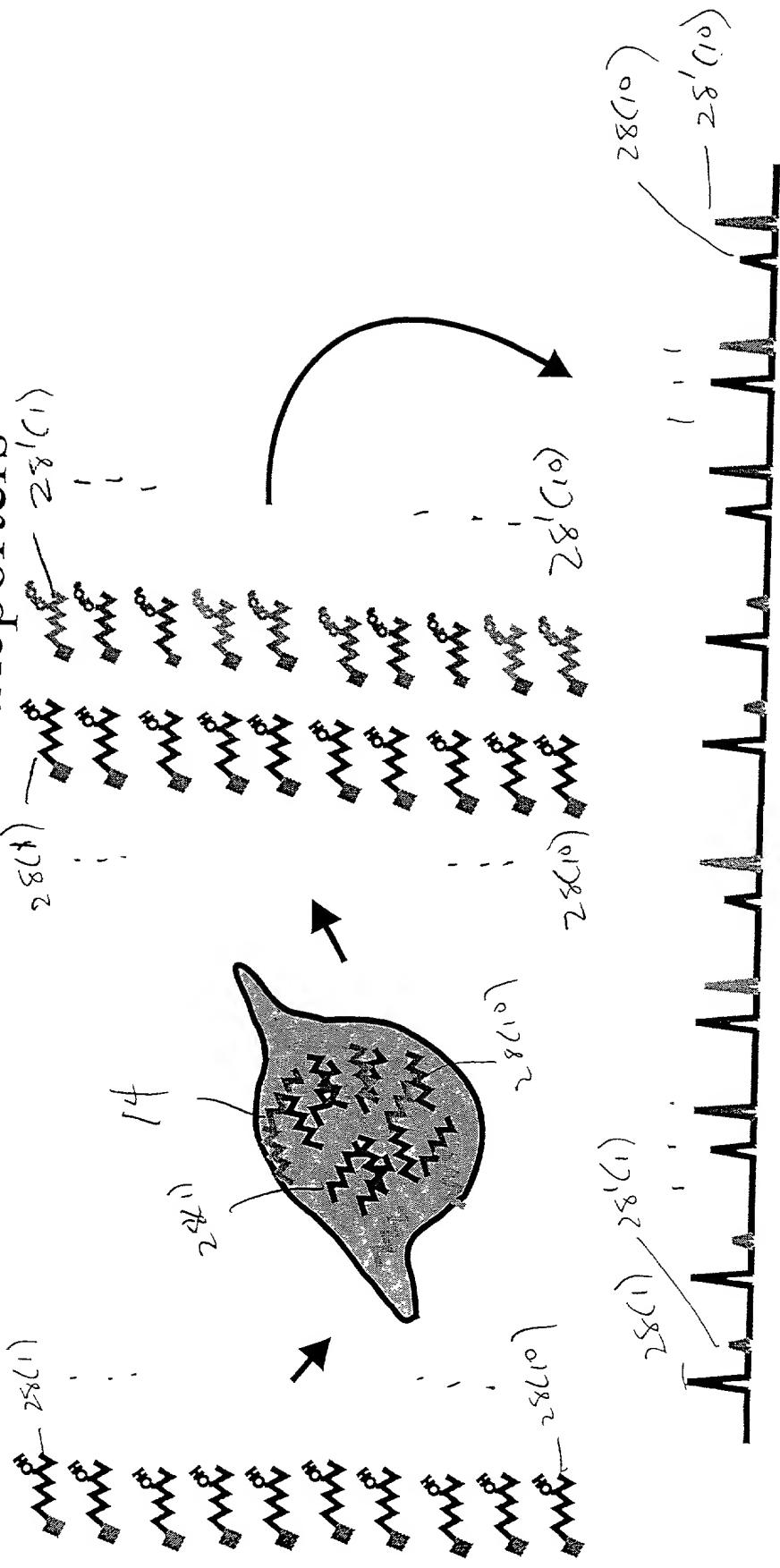


Fig. 18

Profiling Signal Transduction Pathways in Cells with Many Reporters

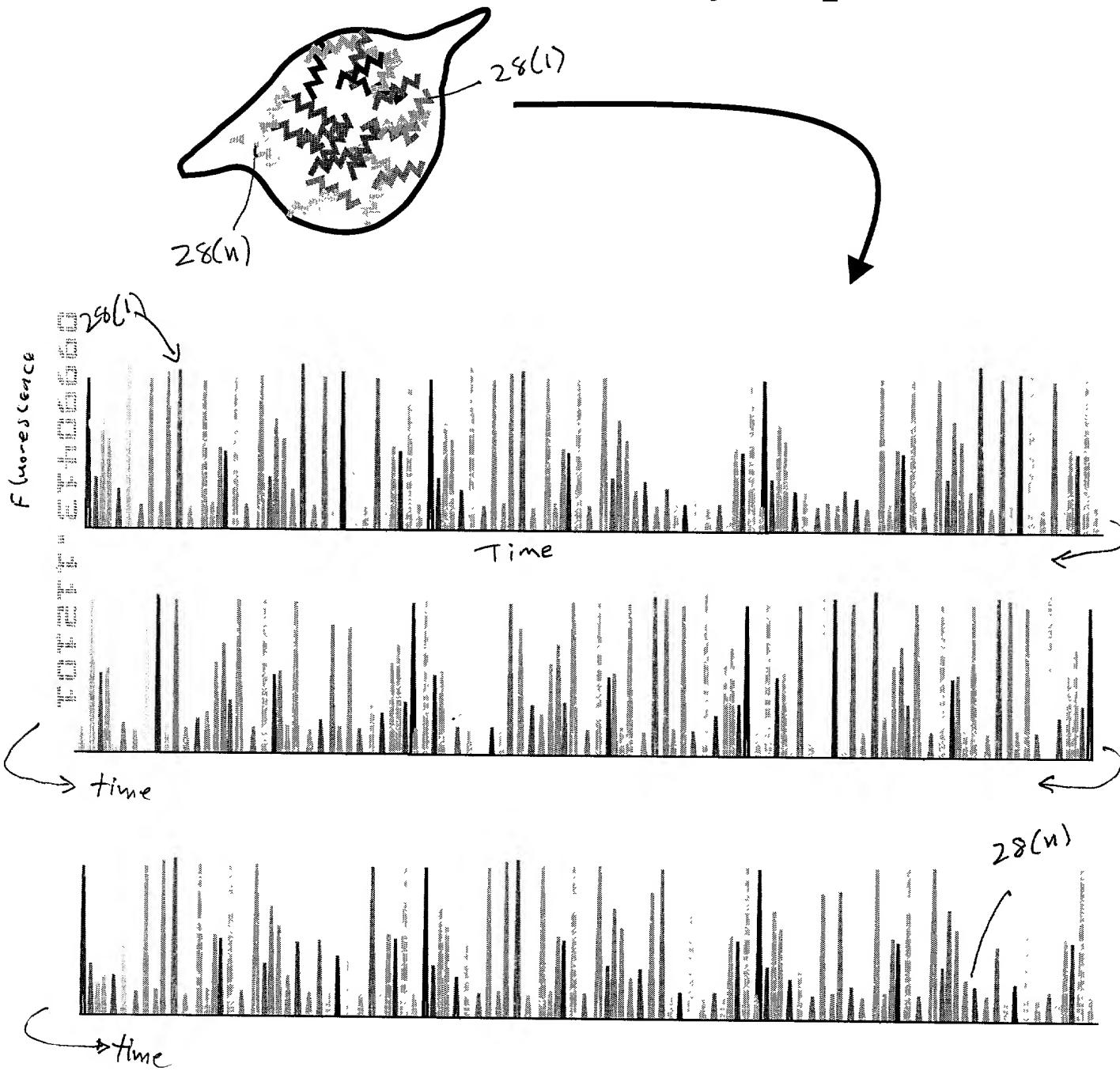


Fig. 19

Applications

- Drug Discovery and Validation

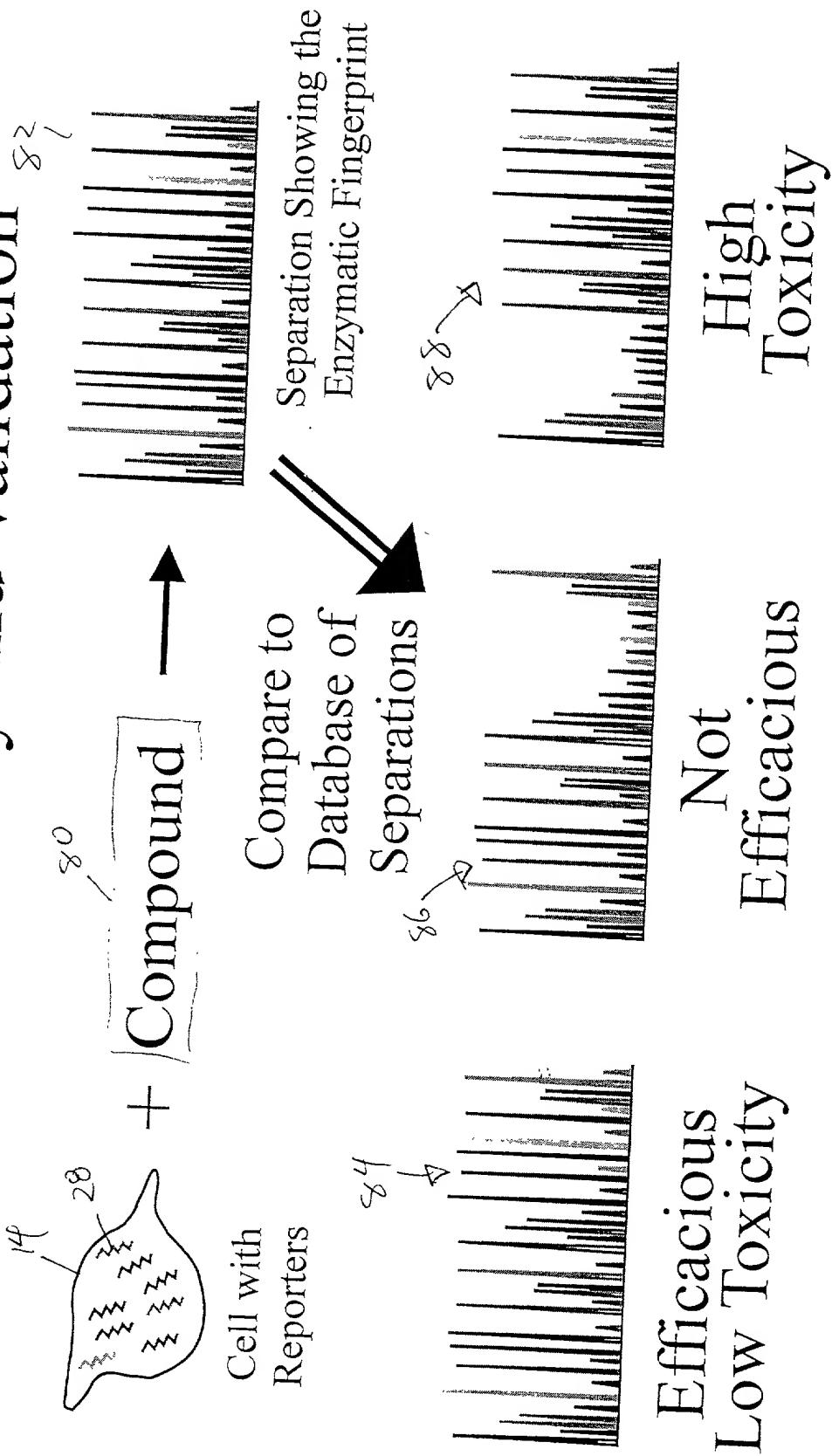
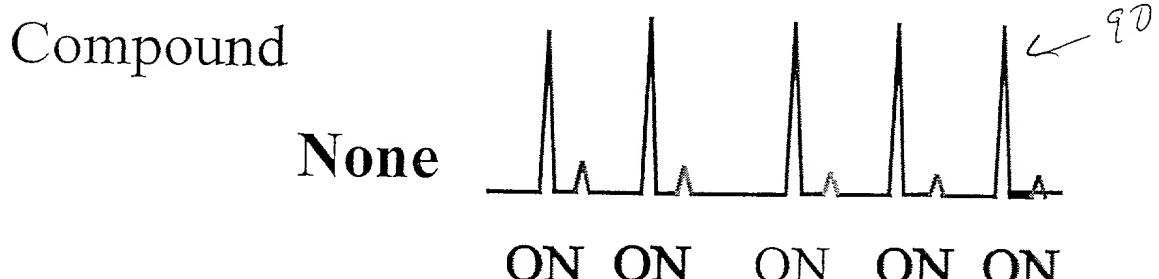
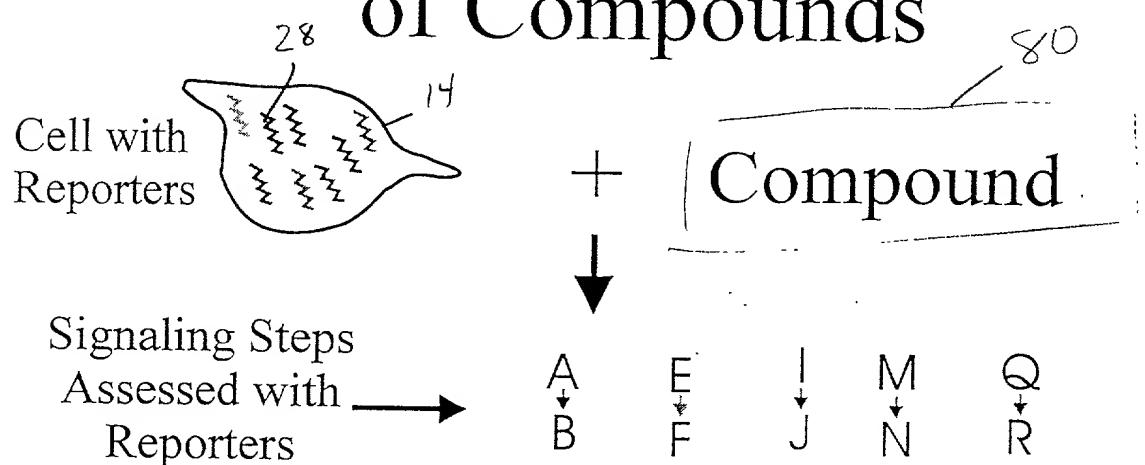


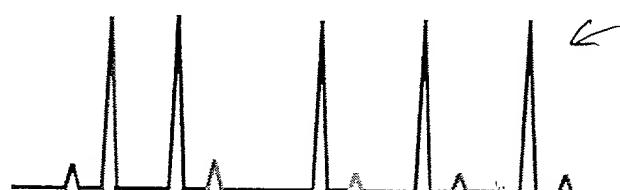
Fig. 20

Identifying the Cellular Targets of Compounds



Y turns Step A to B Off

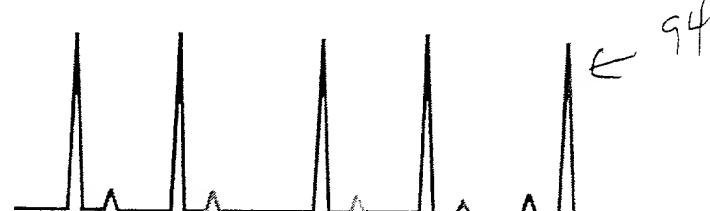
Y



OFF ON ON ON ON

Z turns Step Q to R Off

Z



ON ON ON ON OFF

Fig. 21

Applications

- Diagnostics and Prognostics

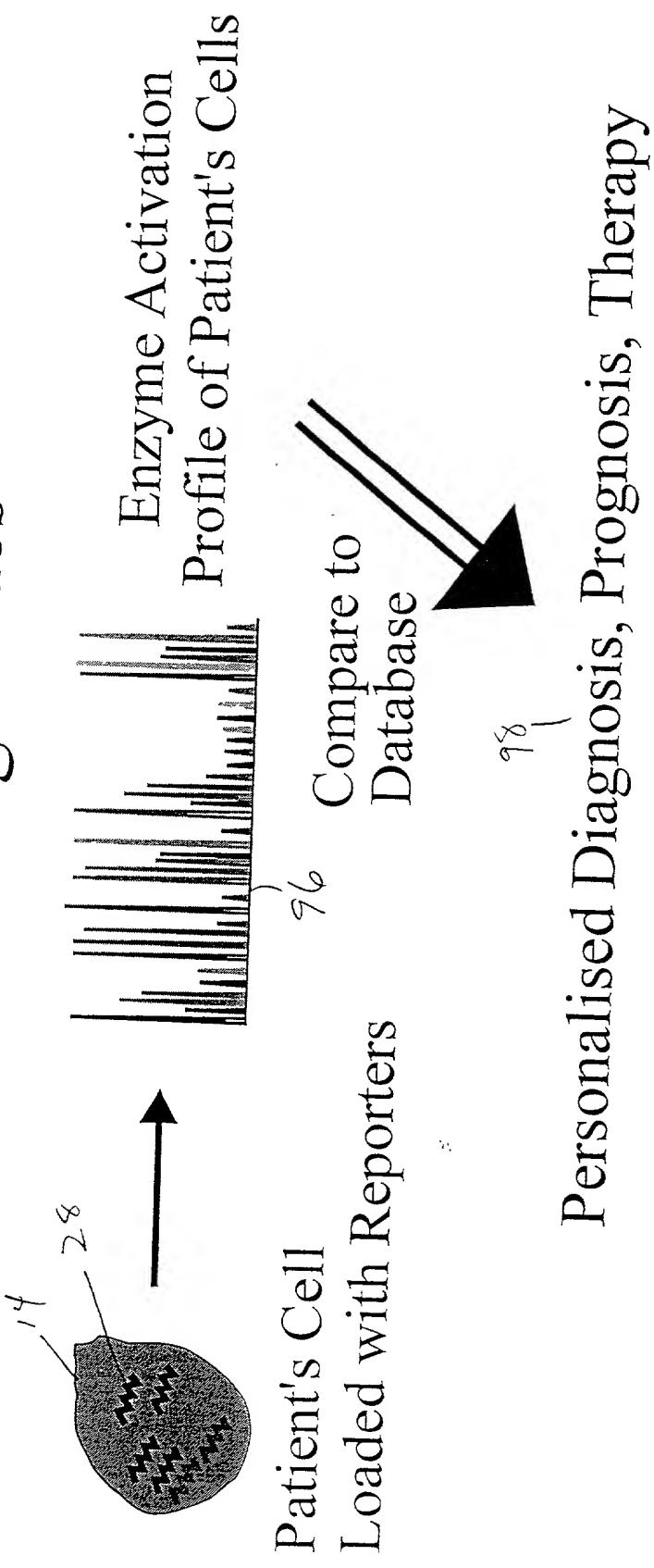


Fig. 22

Identifying and Targeting Pre-Disease or Disease States

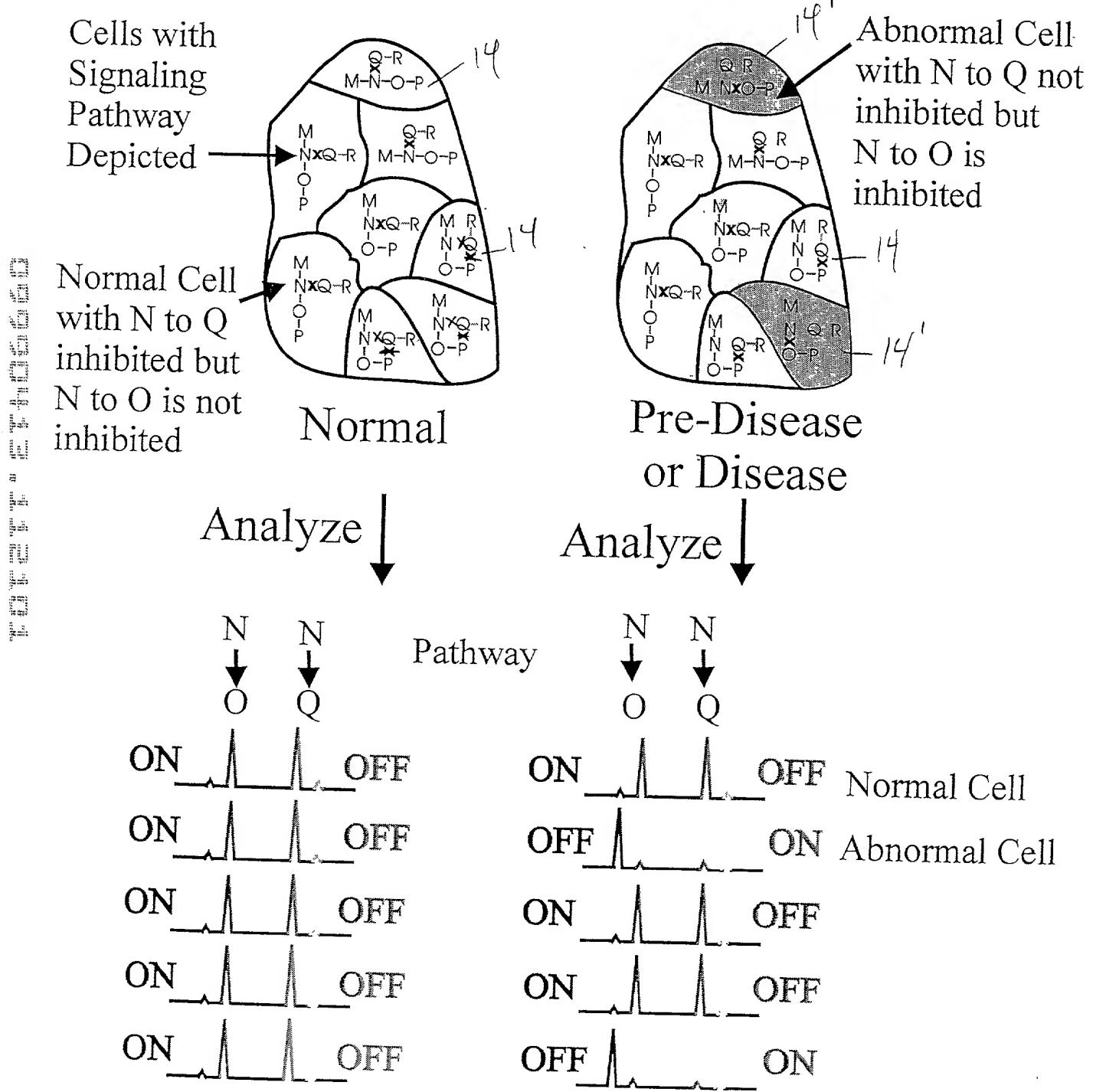
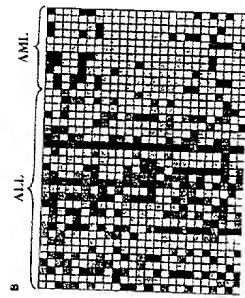


Fig. 23

Analysis of Biologic Systems



DNA Arrays

Mass Spec.,
Protein Arrays

Protein Activity
Maps

Genomics

Proteomics

Signaling

Fig. 24

Serial Analysis of Cells

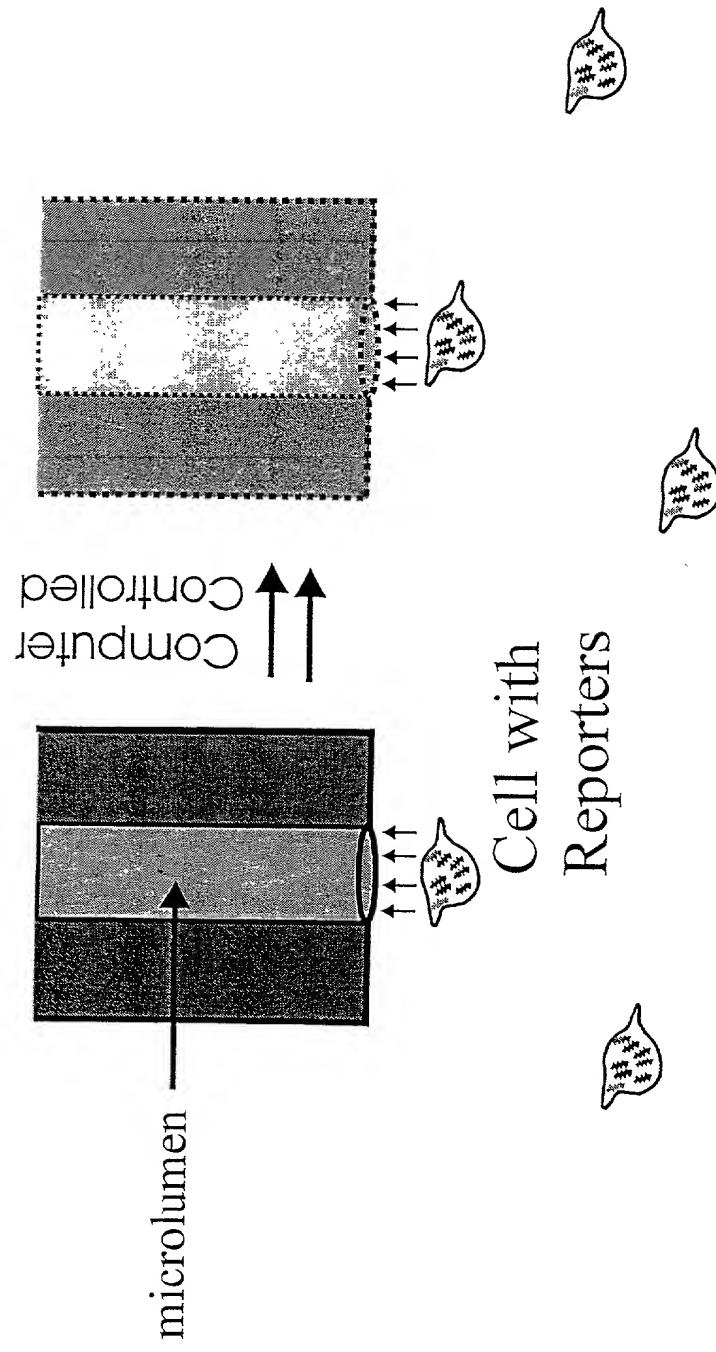
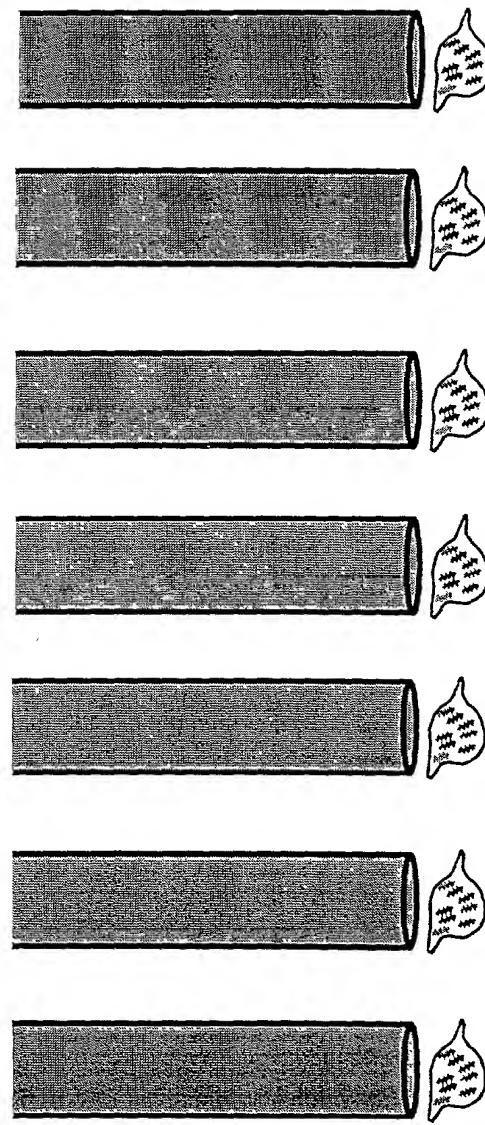


Fig. 25

Parallel Processing of Cells-

Arrays of Separation Channels



Computer-control of microlumen alignment over cells, lysis, and/or other steps.